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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,509	07/05/2001	David Baltimore	A-68798-1/RFT/DHR	4157

7590 11/08/2004

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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/900,509	BALTIMORE ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. This action is in response to Applicants' response filed on June 30, 2004. Currently, claims 1-10 and 12-13 are pending and are rejected herein. This action contains rejections that are not necessitated by Applicants' amendments and therefore, this action is made NON-FINAL. Furthermore, the 102 rejection of Kusher has been withdrawn in view of Applicants' argument that Kushner does not teach, "introducing a plurality of candidate agents." Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-4 and 6-9 are rejected under 35 U.S.C. 102(e)(1) as being anticipated by Glimcher et al. (USPN 5,958,671).

Regarding Claim 1, Glimcher teaches a method for screening for an agent that modulates transcription factor activity, comprising:

(i) providing a cell comprising a transcription factor of interest and a vector comprising a binding site for said transcription factor of interest operatively linked to a reporter gene;

(ii) introducing a plurality of candidate agents to said cell; and

(iii) determining the activity of said transcription factor, wherein a change in activity between the presence and absence of said candidate agents indicates the presence of an agent which modulates transcription factor activity. See cols. 3-4, 6-19, 31-34 and Examples 1-7.

With respect to step (ii), see e.g., col. 4, lines 15-31 and lines 54-64; col. 8, lines 42-48; col. 12, lines 1-46; col. 12, line 62 to col. 13, line 6; col. 18, line 61 to col. 19, line 1; col. 34, lines 22-33; teaching methods for screening for a plurality of compounds that modulate the expression and/or activity of the transcription factor in a cell.

Regarding Claim 2, Glimcher teaches the agent can comprise cDNAs. See col. 3, lines 53-57; col. 8, lines 61-66; col. 12, lines 1-33; col. 13, lines 7-14; col. 13, line 55 to col. 14, line 58; col. 18, lines 30-51; col. 20, lines 49-55, col. 33 and Examples 1-3.

Regarding Claim 3, Glimcher teaches introducing into said cell a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency. See column 5, lines 29-61 and Figures 3-4, for example.

Regarding Claim 4, Glimcher teaches the reporter gene is a luciferase gene. See col. 32, lines 22-28.

Regarding Claims 6-7, Glimcher teaches the activity is inhibited or stimulated. See cols. 3-4 and 8-19, for example.

Regarding Claims 8-9, Glimcher teaches the cell can be a mammalian cell and the expression vector is a mammalian expression vector. See cols. 9-11.

Glimcher also teaches the agent used in the claimed method can comprise a variety of agents, including nucleic acids encoding proteins (see col. 3, lines 53-57; col. 8, lines 61-66; col.

19, line 15; col. 20, line 49-55, for example), including cDNAs (e.g., col. 12, line 33-36, for example). Furthermore, Glimcher teaches a variety of reporter genes are known in the art and are suitable for use in the claimed screening assays. See col. 32, lines 36-42.

Applicants' Arguments

Applicants' argue Glimcher does not teach introducing a plurality of candidate agents to the cell. See page 6 of Applicants' response. Furthermore, Applicants' argue Glimcher does not teach the limitations of Claims 2 and 3 and newly amended Claim 10.

Response to Applicants' Arguments

Applicants' arguments have been considered, but are not persuasive because Glimcher teaches introducing a plurality of candidate agents to the cell and the limitations of Claims 2 and 3. See above. Applicants' argument with respect to Claim 10 is persuasive.

4. Claims 1 and 3-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Kushner et al. (WO 99/11760).

Regarding Claim 1, Kushner teaches a method for screening for an agent that modulates transcription factor activity, comprising:

(i) providing a cell comprising a transcription factor of interest and a vector comprising a binding site for said transcription factor of interest operatively linked to a reporter gene;

(ii) introducing a plurality of candidate agents to said cell; and

(iii) determining the activity of said transcription factor, wherein a change in activity between the presence and absence of said candidate agents indicates the presence of an agent which modulates transcription factor activity. See abstract and pages 3-6, 9-12, 16-17, 20, 22 and 31, for example.

With respect to step (ii), see pages 3, line 5 to page 6, line 1; page 16, lines 22-30; page 20, lines 8-13 and pages 13-14; teaching methods for screening for a plurality of compounds that modulate the expression and/or activity of the transcription factor in a cell.

Regarding Claim 3, Kushner teaches introducing into said cell a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency. See pages 33-34 and Figures 2-4, for example.

Regarding Claim 4, Kushner teaches the reporter gene is a luciferase gene. See page 3, line 25.

Regarding Claim 5, Kushner teaches the reporter gene encodes a fluorescent protein (e.g., GFP). See page 3, lines 26-27.

Regarding Claims 6-7, Kushner teaches the activity is inhibited or stimulated. See pages 3-6, 9-10 and 16, for example.

Regarding Claims 8-9, Kushner teaches the cell can be a mammalian cell and the expression vector is a mammalian expression vector. See page 6, lines 29-30 and pages 22-24, for example.

Kushner also teaches that any compounds can be screened according to the invention, especially those with anti-estrogenic activity. See pages 4 and 31.

5. Claims 1-2, 4-10 and 12-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Cen et al. (US 2003/0170656).

Regarding Claim 1, Cen teaches a method for screening for an agent that modulates transcription factor activity, comprising:

(i) providing a cell comprising a transcription factor of interest and a vector comprising a

binding site for said transcription factor of interest operatively linked to a reporter gene;

(ii) introducing a plurality of candidate agents to said cell; and

(iii) determining the activity of said transcription factor, wherein a change in activity between the presence and absence of said candidate agents indicates the presence of an agent which modulates transcription factor activity. See abstract and paragraphs 4-5, 14, 16-19, 21-22, 25, 35, 52, 58, 60-61, 67, 75-76, 134-135, 142 and pages 19-21, for example.

With respect to step (ii), see paragraphs 18-19, 48, 50, 67, 135; teaching methods for screening for a plurality of compounds that modulate the expression and/or activity of the transcription factor in a cell.

Regarding Claim 2, Cen teaches the agent can comprise cDNAs. See paragraphs 17, 50, 74, 127-128, 132, for example.

Regarding Claim 4, Cen teaches the reporter gene is a luciferase gene. See paragraph 61.

Regarding Claim 5, Cen teaches the reporter gene encodes a fluorescent protein (e.g., GFP). See paragraph 61.

Regarding Claims 6-7, Cen teaches the activity is inhibited or stimulated. See paragraphs 16 and 21-22, for example.

Regarding Claims 8-9, Cen teaches the cell can be a mammalian cell and the expression vector is a mammalian expression vector. See paragraph 25, 35, 49-50, 69 and 112-115, for example.

Regarding Claims 10 and 12-13, Cen teaches the re-screening steps comprising dividing the plurality of candidate agents into subsets each containing an individual candidate (e.g., in a well), introducing said individual candidate agent into an other cell, wherein said other cell

comprises a transcription factor and a vector comprising a binding site for a transcription factor operably linked to a reporter gene, and determining the activity of said transcription factor, wherein the dividing of said plurality of candidate agents and screening is repeated until an individual candidate agent which modulates transcription factor activity is identified. See paragraphs 76, 132-135 and Examples 9-11, for example.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cen et al. (US 2003/0170656), as applied to claims 1-2, 4-10 and 12-13 above, and further in view of Kushner et al. (Pub No. US2002/0098477).

The teachings of Cen are presented above. Cen teaches the co-culturing of the cell comprising the transcription factor of interest with a control plasmid, but does not specifically exemplify, introducing into said cell a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency.

However, Kushner teaches that it is advantageous to introduce into said cell (comprising the transcription factor of interest and a vector comprising a binding site for said transcription factor of interest operatively linked to a reporter gene) a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency. See paragraph 100, for example.

Accordingly, in view of the teachings of Kushner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Cen so as to have introduced into said cell (comprising the transcription factor of interest and a vector comprising a binding site for said transcription factor of interest operatively linked to a reporter gene) a control plasmid comprising a constitutively expressed gene. One of ordinary skill in the art would have been motivated to modify the teachings of Cen to have introduced into said cell (comprising the transcription factor of interest and a vector comprising a binding site for said transcription factor of interest operatively linked to a reporter gene) a control plasmid comprising a constitutively expressed gene, in order to monitor transfection efficiency.

9. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Glimcher et al. (USPN 5,958,671), as applied to claims 1-4 and 6-9 above, and further in view of Kushner et al. (Pub No. US2002/0098477).

The teachings Glimcher et al. are presented above. Glimcher teaches "a variety of reporter genes are known in the art and are suitable for use in the screening assays of the invention," including luciferase, but does not exemplify the use of a fluorescent protein. See col. 32, lines 22-23.

However, Kushner teaches that using green fluorescent protein is advantageous, since the green fluorescent protein provides an "easily assayable product." See page 7, paragraph 80. Kushner also teaches

Accordingly, in view of the teachings of Kushner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Glimcher so as to have used the green fluorescent protein as a reporter gene. One of ordinary skill in the art would have been motivated to modify the teachings of Glimcher to have used a green fluorescent protein as a reporter gene, in order to achieve the benefits stated by Kushner of providing an "easily assayable product" for detection purposes.

Applicants' Arguments

Applicants' argue Glimcher does not teach introducing a plurality of candidate agents to the cell and therefore, the combination of Glimcher and Kushner do not teach all of the claim limitatios. See page 9 of Applicants' response.

Response to Applicants' Arguments

Applicants' argument has been considered, but is not persuasive because Glimcher does teach introducing a plurality of candidate agents to the cell. See above.

10. Claims 10 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glimcher et al. (USPN 5,958,671), as applied to claims 1-4 and 6-9 above, in view of Cen et al. (US 2003/0170656).

The teachings of Glimcher are presented above. Glimcher does not exemplify the re-screening method steps of Claims 10 and 12-13.

However, Cen teaches performing the re-screening methods of Claims 10 and 12-13 is advantageous for determining the specificity of the compounds that modulate transcription factor activity. See paragraphs 76, 132-135 and Examples 9-11, for example.

Accordingly, in view of the teachings of Cen, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Glimcher so as to have performed the re-screening methods of Claims 10 and 12-13. One of ordinary skill in the art would have been motivated to modify the teachings of Glimcher to have performed the re-screening methods of Claims 10 and 12-13, in order to achieve the benefits of determining the specificity of the compounds that modulate transcription factor activity, and thereby identifying an individual candidate agent that modulates transcription factor activity.

11. Claims 10 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kushner et al. (WO 99/11760), as applied to claims 1 and 3-9 above, in view of Cen et al. (US 2003/0170656).

The teachings of Kushner are presented above. Kushner does not exemplify the re-screening method steps of Claims 10 and 12-13.

However, Cen teaches performing the re-screening methods of Claims 10 and 12-13 is advantageous for determining the specificity of the compounds that modulate transcription factor activity. See paragraphs 76, 132-135 and Examples 9-11, for example.

Accordingly, in view of the teachings of Cen, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Kushner so as to have performed the re-screening methods of Claims 10 and 12-13. One of ordinary skill in the art would have been motivated to modify the teachings of Kushner to have performed the re-screening methods of Claims 10 and 12-13, in order to achieve the benefits of determining the specificity of the compounds that modulate transcription factor activity, and thereby identifying an individual candidate agent that modulates transcription factor activity.

Conclusion

12. No claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Alexander H. Spiegler
November 5, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
11/8/04